

What Is Claimed Is:

1. An isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence at least 95% identical to a sequence selected from the group consisting of:

- (a) a nucleotide sequence encoding a polypeptide comprising amino acids from about 1 to about 750 in SEQ ID NO:1;
- (b) a nucleotide sequence encoding a polypeptide comprising amino acids from about 1 to about 750 in SEQ ID NO:1;
- (c) a nucleotide sequence encoding a polypeptide comprising amino acids from about 1 to about 750 in SEQ ID NO:1;
- (d) a nucleotide sequence encoding a polypeptide having the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. PTA-349;
- (e) a nucleotide sequence encoding the mature TR13 polypeptide having the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. PTA-349;
- (f) a nucleotide sequence encoding a polypeptide comprising amino acids from about 1 to about 231 in SEQ ID NO:61;
- (g) a nucleotide sequence encoding a polypeptide comprising amino acids from about 2 to about 231 in SEQ ID NO:61;
- (h) a nucleotide sequence encoding a polypeptide comprising amino acids from about 1 to about 138 in SEQ ID NO:61;
- (i) a nucleotide sequence encoding a polypeptide having the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. PTA-348;
- (j) a nucleotide sequence encoding a polypeptide comprising amino acids 1 to 226 of SEQ ID NO:5;
- (k) a nucleotide sequence encoding the TR14 extracellular domain;
- (l) a nucleotide sequence encoding the TR14 transmembrane domain;
- (m) a nucleotide sequence encoding the TR14 intracellular domain;

- (n) a nucleotide sequence encoding the TR14 receptor extracellular and intracellular domains with all or part of the transmembrane domain deleted;
- (o) a nucleotide sequence encoding a polypeptide comprising amino acids from about 1 to about 1001 in SEQ ID NO:40;
- (p) a nucleotide sequence encoding a polypeptide comprising amino acids from about 2 to about 1001 in SEQ ID NO:40;
- (q) a nucleotide sequence encoding a polypeptide comprising amino acids from about 42 to about 1001 in SEQ ID NO:40;
- (r) a nucleotide sequence encoding a polypeptide having the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. PTA-507;
- (s) a nucleotide sequence encoding the mature TR13 polypeptide having the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. PTA-507;
- (t) a nucleotide sequence encoding the TR13 extracellular domain;
- (u) a nucleotide sequence encoding the TR13 transmembrane domain;
- (v) a nucleotide sequence encoding the TR13 intracellular domain;
- (w) a nucleotide sequence encoding the TR13 receptor extracellular and intracellular domains with all or part of the transmembrane domain deleted; and
- (x) a nucleotide sequence complementary to any of the nucleotide sequences in (a), (b), (c), (d), (e), (f), (g), (h), (i), (j), (k), (l), (m), (n), (o), (p), (q), (r), (s), (t), (u), (v), or (w).

2. The nucleic acid molecule of claim 1, wherein said polynucleotide has the nucleotide sequence in SEQ ID NO:1.

3. The nucleic acid molecule of claim 1, wherein said polynucleotide has the nucleotide sequence in SEQ ID NO:60.

4. The nucleic acid molecule of claim 1, wherein said polynucleotide has the nucleotide sequence in SEQ ID NO:39.

5. The nucleic acid molecule of claim 1, wherein said polynucleotide has the nucleotide sequence in SEQ ID NO:1 encoding the TR13 receptor having the amino acid sequence in SEQ ID NO:2.

6. The nucleic acid molecule of claim 1, wherein said polynucleotide has the nucleotide sequence in SEQ ID NO:60 encoding the TR14 receptor having the amino acid sequence in SEQ ID NO:61.

7. The nucleic acid molecule of claim 1, wherein said polynucleotide has the nucleotide sequence in SEQ ID NO:39 encoding the TR14 receptor having the amino acid sequence in SEQ ID NO:40.

8. The nucleic acid molecule of claim 1, wherein said polynucleotide has the nucleotide sequence in SEQ ID NO:1 encoding the mature TR13 receptor having the amino acid sequence in SEQ ID NO:2.

9. The nucleic acid molecule of claim 1, wherein said polynucleotide has the nucleotide sequence in SEQ ID NO:60 encoding the extracellular domain of the TR14 receptor having the amino acid sequence in SEQ ID NO:61.

10. The nucleic acid molecule of claim 1, wherein said polynucleotide has the nucleotide sequence in SEQ ID NO:39 encoding the mature TR13 receptor having the amino acid sequence in SEQ ID NO:40.

11. The nucleic acid molecule of claim 1, wherein said polynucleotide has the complete nucleotide sequence of the cDNA clone contained in ATCC Deposit No. PTA-349.

12. The nucleic acid molecule of claim 1, wherein said polynucleotide has the complete nucleotide sequence of the cDNA clone contained in ATCC Deposit No. PTA-348.

13. The nucleic acid molecule of claim 1, wherein said polynucleotide has the complete nucleotide sequence of the cDNA clone contained in ATCC Deposit No. PTA-507.

14. The nucleic acid molecule of claim 1, wherein said polynucleotide has the nucleotide sequence encoding the TR13 receptor having the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. PTA-349.

15. The nucleic acid molecule of claim 1, wherein said polynucleotide has the nucleotide sequence encoding the TR14 receptor having the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. PTA-348.

16. The nucleic acid molecule of claim 1, wherein said polynucleotide has the nucleotide sequence encoding the TR13 receptor having the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. PTA-507.

17. The nucleic acid molecule of claim 1, wherein said polynucleotide has the nucleotide sequence encoding the mature TR13 receptor having the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. PTA-349.

18. The nucleic acid molecule of claim 1, wherein said polynucleotide has the nucleotide sequence encoding the extracellular domain of the TR14 receptor having the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. PTA-348.

19. The nucleic acid molecule of claim 1, wherein said polynucleotide has the nucleotide sequence encoding the mature TR13 receptor having the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. PTA-507.

20. An isolated nucleic acid molecule comprising a polynucleotide which hybridizes under stringent hybridization conditions to a polynucleotide having a nucleotide sequence identical to a nucleotide sequence in (a), (b), (c), (d), (e), (f), (g), (h), (i), (j), (k), (l), (m), (n), (o), (p), (q), (r), (s), (t), (u), (v), (w), or (x) of claim 1, wherein said polynucleotide which hybridizes does not hybridize under stringent hybridization conditions to a polynucleotide having a nucleotide sequence consisting of only A residues or of only T residues.

21. An isolated nucleic acid molecule comprising a polynucleotide which encodes the amino acid sequence of an epitope-bearing portion of a TR13 receptor having an amino acid sequence in (a), (b), (c), (d), (e), (f), (g), (h), (i), (j), (k), (l), (m), (n), (o), (p), (q), (r), (s), (t), (u), (v), (w), or (x) of claim 1.

22. An isolated nucleic acid molecule comprising a polynucleotide which encodes the amino acid sequence of an epitope-bearing portion of a TR14 receptor having an amino acid sequence in (a), (b), (c), (d), (e), (f), (g), (h), (i), (j), (k), (l), (m), (n), (o), (p), (q), (r), (s), (t), (u), (v), (w), or (x) of claim 1.

23. The isolated nucleic acid molecule of claim 21, which encodes an epitope-bearing portion of a TR13 receptor selected from the group consisting of: a polypeptide comprising amino acid residues from about 2 to about 170 in SEQ ID NO:2; a polypeptide comprising amino acid residues from about 210 to about 318 in SEQ ID NO:2; a polypeptide comprising amino acid residues from about 343 to about 480 in SEQ ID NO:2; a polypeptide comprising amino acid residues from about 548 to about 592 in SEQ ID NO:2; or a polypeptide comprising amino acid residues from about 632 to about 742 in SEQ ID NO:2, or a polypeptide comprising amino acid residues from about 1 to about 262 in SEQ ID NO:40, or a polypeptide comprising amino acid residues from about 264 to

about 423 in SEQ ID NO:40, or a polypeptide comprising amino acid residues from about 437 to about 789 in SEQ ID NO:40, or a polypeptide comprising amino acid residues from about 791 to about 1001 in SEQ ID NO:40.

24. The isolated nucleic acid molecule of claim 22, which encodes an epitope-bearing portion of a TR14 receptor selected from the group consisting of: a polypeptide comprising amino acid residues from about 2 to about 24 in SEQ ID NO:5; a polypeptide comprising amino acid residues from about 42 to about 52 in SEQ ID NO:5; a polypeptide comprising amino acid residues from about 80 to about 115 in SEQ ID NO:5; or a polypeptide comprising amino acid residues from about 155 to about 226 in SEQ ID NO:5.

25. The isolated nucleic acid molecule of claim 1, which encodes the TR14 receptor extracellular domain.

26. The isolated nucleic acid molecule of claim 1, which encodes the TR14 receptor transmembrane domain.

27. The isolated nucleic acid molecule of claim 1, which encodes the TR14 receptor intracellular domain.

28. The isolated nucleic acid molecule of claim 1, which encodes the TR13 receptor extracellular domain.

29. The isolated nucleic acid molecule of claim 1, which encodes the TR13 receptor transmembrane domain.

30. The isolated nucleic acid molecule of claim 1, which encodes the TR13 receptor intracellular domain.

31. An isolated nucleic acid molecule comprising a polynucleotide having a sequence at least 95% identical to a sequence selected from the group consisting of:

- (a) the nucleotide sequence of clone HETAQ12R (SEQ ID NO:8);
- (b) the nucleotide sequence of clone HETAK82R (SEQ ID NO:9);
- (c) the nucleotide sequence of clone HETBH18R (SEQ ID NO:10);
- (d) the nucleotide sequence of clone HEPAB26R (SEQ ID NO:11);
- (e) the nucleotide sequence of clone HETAN38R (SEQ ID NO:12);
- (f) the nucleotide sequence of clone HPWDD30R (SEQ ID NO:13);
- (g) the nucleotide sequence of clone HETAT05R (SEQ ID NO:14);
- (h) the nucleotide sequence of clone HETDQ39R (SEQ ID NO:15);
- (i) the nucleotide sequence of clone HETEM84R (SEQ ID NO:16);
- (j) the nucleotide sequence of clone HSIDV42R (SEQ ID NO:17); and
- (k) a nucleotide sequence complementary to any of the nucleotide sequences in (a), (b), (c), (d), (e), (f), (g), (h), (i), or (j) above.

32. An isolated nucleic acid molecule comprising a polynucleotide having a sequence at least 95% identical to a sequence selected from the group consisting of:

- (a) the nucleotide sequence of clone HSABD50R (SEQ ID NO:18);
- (b) the nucleotide sequence of clone HTXMX53R (SEQ ID NO:19);
- (c) the nucleotide sequence of clone HE2OR74R (SEQ ID NO:20);
- (d) the nucleotide sequence of clone HMSHK47R (SEQ ID NO:21);
- (e) the nucleotide sequence of clone HMSHK59R (SEQ ID NO:22);
- and
- (f) a nucleotide sequence complementary to any of the nucleotide sequences in (a), (b), (c), (d), or (e) above.

33. An isolated nucleic acid molecule comprising a polynucleotide having a sequence at least 95% identical to a sequence selected from the group consisting of:

- (a) the nucleotide sequence of clone HETAQ12R (SEQ ID NO:48);
- (b) the nucleotide sequence of clone HETAK82R (SEQ ID NO:49);

- (c) the nucleotide sequence of clone HETBM71R (SEQ ID NO:50);
- (d) the nucleotide sequence of clone HETBH18R (SEQ ID NO:51);
- (e) the nucleotide sequence of clone HEPAB26R (SEQ ID NO:52);
- (f) the nucleotide sequence of clone HETAN38R (SEQ ID NO:53);
- (g) the nucleotide sequence of clone HPWDD30R (SEQ ID NO:54);
- (h) the nucleotide sequence of clone HETAT05R (SEQ ID NO:55);
- (i) the nucleotide sequence of clone HETDQ39R (SEQ ID NO:56);
- (j) the nucleotide sequence of clone HPWBL93R (SEQ ID NO:57);
- (k) the nucleotide sequence of clone HETEM84R (SEQ ID NO:58);
- (l) the nucleotide sequence of clone HSIDV42R (SEQ ID NO:59); and
- (m) a nucleotide sequence complementary to any of the nucleotide sequences in (a), (b), (c), (d), (e), (f), (g), (h), (i), (j), (k), (l) or (m) above.

34. A method for making a recombinant vector comprising inserting an isolated nucleic acid molecule of claim 1 into a vector.

35. A recombinant vector produced by the method of claim 34.

36. A method of making a recombinant host cell comprising introducing the recombinant vector of claim 35 into a host cell.

37. A recombinant host cell produced by the method of claim 36.

38. A recombinant method for producing a TR13 polypeptide, comprising culturing the recombinant host cell of claim 37 under conditions such that said polypeptide is expressed, and recovering said polypeptide.

39. A recombinant method for producing a TR14 polypeptide, comprising culturing the recombinant host cell of claim 37 under conditions such that said polypeptide is expressed, and recovering said polypeptide.

40. An isolated TR13 polypeptide having an amino acid sequence at least 95% identical to a sequence selected from the group consisting of:

- (a) amino acids from about 1 to about 750 in SEQ ID NO:2;
- (b) amino acids from about 2 to about 750 in SEQ ID NO:2;
- (c) amino acids from about 1 to about 1001 in SEQ ID NO:40;
- (d) amino acids from about 2 to about 1001 in SEQ ID NO:40;
- (e) the amino acid sequence of the TR13 polypeptide having the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. PTA-349,
- (f) the amino acid sequence of the TR13 polypeptide having the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. PTA-507,
- (g) the amino acid sequence of the mature TR13 polypeptide having the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. PTA-349;
- (h) the amino acid sequence of the mature TR13 polypeptide having the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. PTA-507; and

(i) the amino acid sequence of an epitope-bearing portion of any one of the polypeptides of (a), (b), (c), (d), (e), (f), (g), or (h).

41. An isolated TR14 polypeptide having an amino acid sequence at least 95% identical to a sequence selected from the group consisting of:

- (a) amino acids from about 1 to about 231 in SEQ ID NO:61;
- (b) amino acids from about 2 to about 231 in SEQ ID NO:61;
- (c) amino acids from about 1 to about 138 in SEQ ID NO:61;
- (d) amino acids from about 156 to about 231 in SEQ ID NO:61;
- (e) the amino acid sequence of the TR14 polypeptide having the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. PTA-348;
- (f) amino acids 73 to 226 of SEQ ID NO:5;

- (g) the amino acid sequence of the TR14 receptor extracellular domain;
- (h) the amino acid sequence of the TR14 receptor transmembrane domain;
- (i) the amino acid sequence of the TR14 receptor intracellular domain;
- (j) the amino acid sequence of the TR14 receptor intracellular and extracellular domains with all or part of the transmembrane domain deleted; and
- (k) the amino acid sequence of an epitope-bearing portion of any one of the polypeptides of (a), (b), (c), (d), (e), (f), (g), (h), (i), or (j).

42. An isolated polypeptide comprising an epitope-bearing portion of the TR13 receptor protein, wherein said portion is selected from the group consisting of: a polypeptide comprising amino acid residues from about 2 to about 170 in SEQ ID NO:2; a polypeptide comprising amino acid residues from about 210 to about 318 in SEQ ID NO:2; a polypeptide comprising amino acid residues from about 343 to about 480 in SEQ ID NO:2; a polypeptide comprising amino acid residues from about 545 to about 592 in SEQ ID NO:2; a polypeptide comprising amino acid residues from about 632 to about 742 in SEQ ID NO:2; a polypeptide comprising amino acid residues from about 1 to about 262 in SEQ ID NO:40; a polypeptide comprising amino acid residues from about 264 to about 423 in SEQ ID NO:40; a polypeptide comprising amino acid residues from about 437 to about 789 in SEQ ID NO:40; a polypeptide comprising amino acid residues from about 791 to about 1001 in SEQ ID NO:40.

43. An isolated polypeptide comprising an epitope-bearing portion of the TR14 receptor protein, wherein said portion is selected from the group consisting of: a polypeptide comprising amino acid residues from about 2 to about 24 in SEQ ID NO:5; a polypeptide comprising amino acid residues from about 42 to 52 in SEQ ID NO:5; a polypeptide comprising amino acid residues from about 80 to about 115 in SEQ ID NO:5; and a polypeptide comprising amino acid residues from about 155 to about 226 in SEQ ID NO:5.

44. An isolated antibody that binds specifically to a TR13 receptor polypeptide of claim 40.

45. An isolated antibody that binds specifically to a TR14 receptor polypeptide of claim 41.

46. A method of treating diseases and disorders associated with the inhibition of apoptosis comprising administering an effective amount of the polypeptide as claimed in claim 40, or an agonist thereof to a patient in need thereof.

47. A method of treating diseases and disorders associated with the inhibition of apoptosis comprising administering an effective amount of the polypeptide as claimed in claim 41, or an agonist thereof to a patient in need thereof.

48. A method of treating diseases and disorders associated with increased apoptosis comprising administering to a patient in need thereof an effective amount of an antagonist of the polypeptide as claimed in claim 40 to a patient in need thereof.

49. A method of treating diseases and disorders associated with increased apoptosis comprising administering to a patient in need thereof an effective amount of an antagonist of the polypeptide as claimed in claim 41 to a patient in need thereof.

50. A method of treating inflammatory diseases and disorders comprising administering to a patient in need thereof an effective amount of an antagonist of the polypeptide as claimed in claim 40.

51. A method of treating inflammatory diseases and disorders comprising administering to a patient in need thereof an effective amount of an antagonist of the polypeptide as claimed in claim 41.

52. A method of treating, preventing, or ameliorating an epithelial disorder comprising administering a TR14 polynucleotide, polypeptide, or agonist to a patient in need of such treatment, prevention, or amelioration.

53. The method of claim 52, wherein said disorder is hypohidrotic ectodermal dysplasia.

54. A method of treating cancer comprising administering an effective amount of an agonist of the polypeptide as claimed in claim 40, to a patient in need thereof.

55. The method of claim 54 wherein the agonist is an anti-TR13 antibody.

56. The method of claim 54 wherein the cancer is a cancer of the gastrointestinal system.

57. The method of claim 54 wherein the cancer is a cancer of the reproductive system.

58. The method of claim 54 wherein the cancer is a cancer of the immune system.

59. A method of preventing cell death, comprising administering an effective amount of the soluble extracellular domain of TR13, to a patient in need thereof.

60. A method of reducing graft rejection, comprising administering an effective amount of the polypeptide as claimed in claim 40, to a patient in need thereof.

61. A method of reducing graft rejection, comprising administering an effective amount of an agonist of the polypeptide as claimed in claim 40, to a patient in need thereof.

62. A method of reducing graft rejection, comprising administering an effective amount of an antagonist of the polypeptide as claimed in claim 40, to a patient in need thereof.

63. A method of inhibiting Fas ligand activity in a patient comprising administering to said patient an effective amount of the polypeptide as claimed in claim 40.